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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/723,000	11/27/2000	Jorg J. Goronzy	07039-170002	4888

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	19

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/723,000	GORONZY ET AL.	
	Examin r	Art Unit	
	Stacy B Chen	1648	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-57 and 60-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-57 and 60-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed September 19, 2003 is acknowledged and entered. Claims 48-57 and 60-62 are pending and examined.

2. The objection to claim 61 is withdrawn in view of Applicant's amendment. The rejection of claims 48-57 and 60-62 under 35 U.S.C. 112, second paragraph, is withdrawn in view of Applicant's persuasive arguments.

Specification

3. The specification, page 14, contains a list of sequences. These sequences appear to match with the sequence listing of the application. The sequences listed on page 14 should be notated with their respective sequence identifiers. Applicant has indicated that they are compliant with the sequence rules. The Office recognizes that the sequences on page 14 are in the sequence listing. However, the specification must provide a SEQ ID number for each sequence in the table on page 14 to show that the sequences correspond to those in the sequence listing. If Applicant has already submitted such an amendment, Applicant is requested to resubmit the amendment.

Claim Rejections - 35 USC § 112

4. Claims 48-57 and 60-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The amended claims recite HLA-DRB1 *0401, *0404, *0405

and *0408 alleles. It is unclear what is meant by " * ". Does this symbol mean that there is a polymorphism in the allele? Clarification is requested.

5. Claims 48-57 and 60-62 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record. The specification, while being enabling for the determination of developing severe disease by detecting the presence or absence of some polymorphisms in the HLA-DRB1 allele, does not reasonably provide enablement for the determination of developing severe disease by detecting the presence or absence of any polymorphism in the HLA-DRB1 allele. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Applicant's amendments and arguments have been carefully considered but fail to persuade. The amendment to claim 48 narrows the scope of the claim, but not to the degree of being fully enabled. The amendment narrows the claim to a method for determining the predisposition of a RA patient to develop severe disease, wherein the method comprises comparing the frequency of $CD4^{+}/CD28^{null}$ cells to a reference frequency, and determining if the patient is predisposed to develop severe disease based on said information and the presence or absence of HLA-DRB1 *0401, *0404, *0405 and *0408. It is unclear what is meant by the "*0401", see 35 U.S.C. 112, second paragraph rejection above. If the term "HLA-DRB1 *0401" means that there is a polymorphism in the HLA-DRB1 0401 allele, then the claims are not enabled for such a broad scope. The breadth of the claims is unreasonable, encompassing the detection of any polymorphism and correlating it to the likelihood of developing severe RA. The specification fails to provide guidance for correlating any random polymorphism to the method

of determining a predisposition to severe RA. The specification sets for three polymorphisms that correlate with RA associated alleles on page 4, lines 18-20. Although Applicant has limited the alleles to 0401, 0404, 0405 and 0408, the claims are enabled for any polymorphism in these alleles.

Claim Rejections - 35 USC § 103

6. Claims 48-57 and 60-62 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Goronzy *et al* (*J. Clin. Investigation, Inc.* 1994, 94:2068-2076) in view of Abril *et al* (*Arthritis Rheum.*, 1998, 40:762) for reasons of record. Applicant's arguments and amendments have been carefully considered but fail to persuade.

Applicant's substantive arguments are primarily directed to the assertion that the prior art of record fails to indicate that $CD4^{+}/CD28^{null}$ frequencies and HLA-DRB1 alleles are independent indicators that should be used together to assess a RA patient's predisposition to develop severe disease. Applicant argues that the prior art does not disclose that $CD4^{+}/CD28^{null}$ T cell counts are independent of the HLA-DRB1 genotype, evidenced by Chapman (*J. Immunology*, 1996, 157:4771-4780) which teaches that $CD4^{+}/CD28^{null}$ frequencies are associated with HLA-DRB1 alleles such as HLA-DRB1 *0401.

In response, the claims are drawn to a method that requires determining $CD4^{+}/CD28^{null}$ frequency and the presence or absence of certain alleles. The argument that the prior art fails to teach that $CD4^{+}/CD28^{null}$ frequency and the presence or absence of certain alleles are independently capable of determining if a patient is predisposed to develop severe disease, is not commensurate in scope with the claims. One of ordinary skill does not need to know that the

two determinations of $CD4^+/CD28^{null}$ frequency and presence/absence of certain alleles are independently capable of determining if a patient is predisposed to develop severe disease to practice the claimed invention. Therefore, the claims remain rejected as obvious over the prior art of record.

Conclusion

7. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 872-9306. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy B. Chen, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday from 7:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SBC

Stacy B. Chen
November 6, 2003

James C. Housel 11/5/03
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
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